Reviewer's report

Title: Clinical, Economic, and Humanistic Burden of Asthma in Canada: A Systematic Review

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Reviewer: Matthew Rank

Reviewer's report:

This is a systematic review of the clinical, economic, and economic burden of asthma in Canada from 2000-2011. The authors conclude that the data from this study can assist those who make decisions about asthma treatment selection and guideline management.

1. Is the question posed by the authors well defined?

This is a descriptive systematic review, with the goal of describing the burden of asthma in Canada from 2000-2011. The stated goals are to have these data be available to those making decisions about asthma treatments in the future. There is not a specific research question or hypothesis stated. The link between their data summary and how this can be used for decisions on asthma treatment could be explained more clearly.

2. Are the methods appropriate and well described?

The methods for systematic review are, in general, well described in this manuscript. They employ the usual standards for a systematic review including an appendix detailing their search strategy, duplicate review, and a quality assessment of the selected articles using previously reported and accepted instruments.

There are some methodological concerns. The major concern is about efforts to detect publication bias. It is unclear what methods were used to assess this. Many of the studies that examine burden of disease are funded by companies which make medicines or drugs to treat these conditions. If a study was conducted and the burden found to be low, it is possible that the study would never be published. It is unclear if the authors made an attempt to find such data. Furthermore, the funding of the studies was not clearly displayed for the reader, especially in the summary tables. The confidence in the estimates of burden, then, may be lower by readers who share this concern. Secondary methodologic concerns regard the heterogeneity of definitions and outcomes in the studies that were identified. The authors make no attempt to synthesize data into a common estimate using meta-analysis methods, presumably due to heterogeneity of study designs. The authors should state whether they attempted this, which could have been an initial goal of the study. Such a summary estimate may prove more useful for those who would use these data to determine guideline or coverage decisions for asthma medications. Another concern is the interpretation of the
humanistic burden; without non-asthmatic normal control groups understanding the attributable humanistic burden of asthma is challenging. It is not clear how many of these studies included non-asthma patients and if the difference between a control and asthma patient was detected and what the mean difference was. A lesser concerns is how initial review was conducted; it is unclear if title or abstract review occurred at the first level of exclusion. Another lesser concern is that the authors do not justify their selection of using the 2000-2011 time period.

3. Are the data sound?

The data presented resulted from a comprehensive search of the published literature. The authors assess and recognize the low quality of many of the studies included, as well as the heterogeneity of definitions used for inclusion/exclusion and outcomes.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

Yes, the authors use and report the standard methods for performing a systematic review.

5. Are the discussion and conclusions well balanced and adequately supported by the data?

The authors speculate about the future need for new asthma treatments in the discussion rather than focus on the heterogeneity of the data and the need for more standardized methods to assess the burden of asthma. The authors make this point in the discussion section “…our study suggests a significant knowledge gap in understanding the comprehensive burden of asthma across Canada.” The discussion should, in my opinion, focus on the gaps that they identified in the data types and study designs (especially the flaws) and put forward study designs, inclusion/exclusion criteria, and outcome reporting methods that they would believe would lead to improved ability to assess asthma burden (and would ultimately allow them to obtain data that could be synthesized into estimates that those who make treatment, guideline, and coverage decisions could rely on). The authors choose, instead, to make a conclusion that the burden is high (a statement that is made in the background section as a fact that is known already) and that new treatments for asthma are needed. The other area in the discussion section that is not addressed is the risk for publication bias. How those making decisions about asthma coverage and guidelines should use these data and how confident they should be in the results of this study are not clearly laid out in the discussion section.

6. Are the limitations of the work clearly stated?

The main concern about publication bias and heterogeneity of the included studies are stated above.

7. Do the authors clearly acknowledge any work upon which they are building,
both published and unpublished?

The authors reference #9, a 2009 review not restricted to Canada that assesses the economic burden of asthma. The authors do not compare their data with the findings and conclusions from this review. How do these findings compare to other countries or other chronic diseases within Canada?

8. Do the title and abstract accurately convey what has been found?
   Yes

9. Is the writing acceptable?

   Yes, the writing is generally clear. The authors could display their results more concisely in tables (the current tables could have less words that could convey the same messages). The text in the results section could be considerably shortened if the tables were used more effectively. Displaying funding source in the tables would also be important.

   Discretionary revisions: Table revisions and minor methodological concerns.

   Minor essential revisions: None

   Major compulsory revisions: Addressing risk of publication bias, restructuring discussion section to focus on gaps and problems with currently available studies so that future studies can be more informative, attempting to report the humanistic burden as attributable to asthma, and establishing a clearer link between the data presented (and the confidence in the estimates) and how someone is deciding about coverage, guidelines, or public health can use this information.

   I have no reason to believe that any duplication or plagiarism occurred or any reason to believe the data has been falsified or manipulated.

   **Level of interest:** An article whose findings are important to those with closely related research interests

   **Quality of written English:** Acceptable

   **Statistical review:** No, the manuscript does not need to be seen by a statistician.

   **Declaration of competing interests:**

   I declare that I have no competing interests.